REMARKS/ARGUMENTS

Claim Status

1. Applicant elected Group I without traverse in a reply filed on March 10, 2005. Claims 11-19 have been withdrawn from further consideration.

2. Claims Pending Claims 1-2,4-29 are pending. Claims 1-2,4-10 and 20-29 have been examined.

Claim Objections

3. The Examiner objected to claims 1, 20 and 28 because of the following informalities: the term "Euphorbaciae" and "Euphorbacea" appear to be misspelled. (Id.) Applicant has corrected the misspellings.

Claim Rejections - 35 U.S.C. § 112 - first paragraph

4. The Examiner rejected claim 1 under 35 U.S.C. §112, first paragraph writing that "the one disclosed embodiment is not representative of the enormous number of plants claimed". (Id.) The Examiner reasons that the "Applicant is not in possession of the claimed plant at the time this application was filed and lacks an adequate written description. "

5. The Applicant has amended claim 1 to recite the species Croton lechleri reflecting the embodiment (i.e. "CGO 110") disclosed in the amended specification. New claim 20 also recites the species Croton lechleri. Support for the species Croton lechleri is based on the current specification and provisional application 60/416,751, attached hereto, from which this application claims benefit. (Appendix A - 60/416,751, "Description" pg. 3)

Claim Rejections - 35 U.S.C. § 112 - second paragraph

6. The Examiner rejected claims 1, 5 and 9 under 35 U.S.C §112, second paragraph, alleging that said claims are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner indicates that Claim 9 recites the limitation "the proanthocyanidin" in line 1 and alleges that there is insufficient antecedent basis for this limitation in the claim. The Examiner then reasons that because claim 9 depends either directly or indirectly upon claims 1 and 5, these claims are also indefinite. (Office Action, pg. 3) It is noted that the Examiner has not cited authority for this proposition - that an indefinite dependent claim renders an intervening prior-dependent claim, or the original independent claim, indefinite. The Applicant requests the legal citation supporting this proposition or a withdrawal of the rejection as to the intervening prior-dependent claim, and the original independent claim.

7. The Applicant has amended claim 9 and cured the alleged defect upon which the Examiner has based the rejection.

Claim Rejections - 35 U.S.C. § 103

8. The Examiner has rejected claims 1-2, 4-10 and 20-29 under 35 U.S.C. 103(a) as being unpatentable over Ubillas et al. ("SP-303, an Antiviral Oligomeric Proanthoycanidin from the Latex of Croton lechleri (Sangre de Drago," Phytomedicine Vol.I/1994, pp. 77-106) in view of Hecker et al. (US 4,716,179) in view of Winter et al. (US 5,474,782). (Office Action, pg. 3)The Examiner asserts that Ubillas discloses “extracting latex from Croton lechleri” by adding isopropanol to the latex. Reportedly, this results in a biphasic mixture which was evaporated to dryness and precipitated with ethyl acetate. (Id.) Ubillas et al. did UV absorption on the solution to show homogeneity.” (Id.) The Examiner goes on to state that “Ubillas et al. did not disclose

wherein the layers were specifically hydrophilic and lipophilic or wherein the drying agent was magnesium sulfate or wherein reducing the proanthcyanidin to about 90% relative to the parent latex." (Id. pg. 3-4) The Examiner indicates that: (i) "Hecker et al. (US 4,716,179) disclose that magnesium sulfate is used as a drying agent"; (ii) Cragoe et al. (US 4,061,643) disclose that magnesium sulfate is used as a drying agent." (Id. pg. 4) The Examiner then concludes that "[o]ne of ordinary skill in the art would have been motivated to separate the layers to obtain the desired solution and then evaporate the organic solvent to obtain a purer form **of the solution**." (Id.) (emphasis added)

9. The Applicant contends that the Examiner has failed to assert a prima facie case under 35 U.S.C. §103. It is well established that a reference anticipates a patent claim only if the reference identically discloses all the limitations of the claim. *Acromed Corp. v. Sofamor Danek Group, Inc.*, 253 F.3d 1371,1383, 59 USPQ2d 1130 (Fed. Cir. 2001). *Corning Glass Works v. Sumitomo Electric U.S.A.*, 868 F.2d 1251, 1259, 9 USPQ2d 1962, 1968 (Fed. Cir. 1989). Moreover, said reference must enable one of skill in the art to make and use the claimed invention. *Transclean Corp. v. Bridgewood Services, Inc.*, 290 F.3d 1364, 62 USPQ2d 1865 (Fed. Cir.2002); *Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1374,58 USPQ2d 1508 (Fed. Cir. 2001); *Chester v. Miller*, 906 F.2d 1574, 1577 n.2, 15 USPQ2d 1333, 1336 n.2 (Fed. Cir. 1990).

1. The Examiner assumes that the process for making the "the solution" disclosed by Ubillas et al. is the same as that for making the Applicant's claimed extract. This is not the case. Ubillas discloses a method of isolating a large proanthocyanidin oligomer from Croton lechleri. (See Ubillas, "Summary" pg. 1.) To achieve its aim, Ubillas discloses in "step 3", that the "residual **aqueous solution** was evaporated to dryness, dissolved in methanol, and precipitated with ethyl acetate (Step 3)." And in "step 4" that "[t]he filtered supernatant was then purified by a combination of ion exchange chromatography and size exclusion chromatography. Using water as the

eluent, alkaloids (primarily taspine) present in the material (Persionos-Purdue et al. {sic}, 1979) were removed from the Step 3 intermediate by ion exchange chromatography on CM-Sephadex C-50. **Further enrichment of the proanthocyanidin polymer-containing fraction** was achieved by connecting a Sephadex G-50 column to the outlet of the CM-Sephadex C-50 column. **With water as the eluent, the proanthocyanidin oligomer adsorbed to the G-SO column while some of the more polar low molecular weight compounds eluted. The bioactive product was then eluted with 15 % aqueous acetone**." (Ubillas, Col. 1, pg. 81.) (emphasis added) Ubillas uses *different steps* to produce a *different end product* than the Applicant claims.

2. The Applicant claims a method for separating and resolving/retaining *the lipophilic components* from species Croton lechleri - not the proanthocyanidin component residing in the residual aqueous solution from the biphasic solution created by the isoproponal and latex solution (See claim 1.) Further, the Examiner does not contend that Hecker *et al.* or Cragoe *et al.* discloses the steps of separating and resolving/retaining the lipophilic components from species Croton lechleri. Accordingly, neither Ubillas nor any of the cited references, disclose (at least) the last two steps of the Applicant's claim. It follows that the cited references fail to establish a prima facie case under 35 U.S.C. §103.

3. Further, neither Ubillas, nor the other cited references, remotely suggest either the goal or the actual steps of separating and resolving the lipophilic components from species Croton lechleri. To establish a *prima facie* case of obviousness; there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; there must be a reasonable expectation of success; and the prior art reference (or references when combined) must teach or suggest all the

claim limitations. See MPEP 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, **not in applicant's disclosure**. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added). Respectfully, the Examiner's analysis contradicts the above case law.

4. The Examiner alleges that, although Ubillas does not disclose reducing the proanthocyanidin contend to about 90% to the parent latex, one would keep extracting the solution until the required solution is obtained. (Office Action, pg 4) And finally that one of ordinary skill would have a reasonable expectation that extracting the latex with an organic solvent would resolve the desired layer. (Id.) Arguably, these assumptions might be true, but only if one were making the Ubillas extract. Put another way, one cannot have a reasonable expectation of success where one is guaranteed to fail. Finally, the Examiner has not expressly alleged that the cited references provide the motivation to combine to render the missing steps or the end goal of separating and resolving the lipophilic components from species Croton lechleri. In fact, the Examiner has cited no origin for the alleged motivation. It follows that the cited references further fail to support a prima facie case of obviousness under 35 U.S.C. §103.

5. Alternatively, if the examiner is relying on personal knowledge to support an allegation of what is known in the art (i.e. a motivation to achieve the end goal of separating and resolving the lipophilic components from species Croton lechleri), the examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the allegation. See 37 CFR 1.104(d)(2). Indeed, the Assignee objects to the use of *his specification* to enable and provide the motivation to modify the prior art reference(s) relied upon in the Examiner's rejection. Finally, the Applicant contends that Ubillas is not modifiable as suggested by the Examiner. Since Ubillas' goal is to isolate the proanthocyanidin oligomer, *which is isolated in the aqueous*

portion of its biphasic mixture. The Examiner's proposed modification of Ubillas would improperly contradict the express goal and teachings of the reference. See MPEP 2143 VI, *citing In re Ratti*, 270 F.2d 810 (CCPA 1959) (if a proposed modification to the prior art would change the principle of operation of the prior art invention being modified, then the teachings are insufficient to render the claimed combination obvious). Simply because prior art references can be combined or modified does not render the combination obvious unless the prior art also suggestions the desirability of the combination. See MPEP 2143 III, *citing In re Mills*, 916 F.2d 680 (Fed. Cir. 1990).

10. Applicant asserts that all the issues of the Examiner's action have been address and requests reconsideration of its claims in light of the amendments and the information herein.

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Respectfully submitted,

Ellis & Venable

Date: June 20, 2006

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APPENDIX A

United States Patent
Bobrowski *et al* October 2, 2002

Methods and preparations of the latex from the *Croton* species

ABSTRACT

The invention herein describes a procedure for organically extracting the lipophilic components from plants of the Family Euphorbaciae, specifically but not limited to the genus *Croton*. The product, hereinafter referred to as AMPSA 100, is deplete of the normal proanthrocyandin content found in the parent material, yet retains its pharmacocological abilities and unlike the parent material, is selectively cytotoxic to cancer cells. The depletion of the proanthocyandin components makes the product more amenable to topical preparations for the benefit of ameliorating both human and animal disease.

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International Class: A61K 009/70; A61K 031/765; A01N 065/00
Field of Search: 424/78.08, 195.1; 520/1; 528/1; 560/69

REFERENCES CITED [Referenced By]

U.S. Patent Documents

5156847	Oct., 1992	Lewis *et al*	424/447
5211944	May., 1993	Tempesta	424/78.08
5474782	Dec., 1995	Winter *et al*	424/443
5494661	Feb., 1996	Tempesta	424/78.38

Other References

Perdue *et al,* J Pharm Sci, 68:124-6, 1979.

Lewis *et al,* Medical and Poisonous Plants of the Tropics, The Netherlands (1987).

Vaisberg *et al,* Planta Med, 55:140-3, 1989.

Itokawa *et al,* Chem Pharm Bull, 39:1041-2, 1991

Pieters *et al,* J Nat Prod, 56:899-06, 1993

Chen *et al,* Planta Med, 60:541-5, 1994

Phillipson, Phytochem, 38:1319-43, 1995.

Desmarchelier *et al,* J Ethnopharm, 58:103-8, 1997

Gabriel *et al,* Am J Physiol, 276:G58-63, 1999

Costa *et al,* Phytochem, 53:851-4, 2000.

Miller *et al,* Am J Gastroint Liv Physiol, 279:G192-200, 2000

Miller *et al,* J Investig dermatol 117: 725-730, 2001

Sandoval *et al,* J Ethnopharmacology 80: 121-129, 2002.

Primary Examiner:

Assistant Examiner:

Attorney, Agent or Firm:

CLAIMS

We claim:

1. A novel method for the extraction of the lipophilic components from plants of the family Euphorbaciae, specifically but not limited to the genus *Croton;*
2. The method in Claim 1 where the sap, latex, bark or materials from Euphorbaciae, or a decoction or tincture thereof, are combined with an organic solvent, preferably but not limited to ethyl acetate;
3. Wherein the combination in Step 3 is sufficiently mixed and/or agitated for a period of time necessary to produce a extract exhibiting a pink color;
4. Wherein Step 3 a drying agent (for example magnesium sulfate, Mg SO4) is added 500mg-5g/L, to remove any water-based chemical contaminants that may contain proanthocyandins and related chemicals, within the organic layer;
5. Wherein the color described in Step 3 is spectrophotometrically determined at a concentration of

2mg/mL v/v ethanol:water in an absorbance wavelength range between 390 nm and 430 nm to be approximately 0.515 Abs Units for the parent material and 0.120 Abs Units for the extracted material (CGO 110);

6. Wherein the solutes from the extract in Step 3 are acquired through methods which include but are not limited to evaporation, spray drying, freeze drying or vacuum drying;
7. Wherein Step 5 yields a fine powder or crystalline material hereinafter referred to as "CGO 110;"
8. Whereas the organic solvent in Step 2 is isopropanol;
9. Whereas the organic solvent in Step 2 is a mixture of Chloroform and Methanol;
10. Wherein the CGO 110 is sufficiently depleted of its proanthocyandin content as to make it suitable for non-discoloring topical applications;
11. Wherein the depletion of proanthocyandin content CGO 110 is measured by UV absorbency in the range of 390nm to 430nm and compared to the parent botanical latex;
12. Wherein the combination of CGO 110 or the unextracted parent material in a fixed ratio (2mg/mL) with *Aloe barbadensis* juice or gel at a UV absorbency range of between 390 nm and 430 nm produces a described "light apple" color (CGO 110: 0.010 Abs units) versus a described "dark chocolate" color (parent material: 0.030 Abs units);
13. Wherein CGO 110 reduces the cytotoxicity to normal cells when compared to its botanical base, yet retains its ability kill cancer cells *in vitro* whereas the parent sangre de grado is not selective in promoting cell death ;
14. Wherein CGO 110 prevents emesis;
15. Wherein CGO 110 blocks the activation of sensory afferent nerves; and,
16. Whereas the ability of said action in Step 14 has application for a variety of human and animal conditions, including but not limited to the ability to negate diarrhea and the sensations of pain, nausea and itch associated with sensory afferent nerve activation.

DESCRIPTION

The present invention describes a the use of organic solvents to obtain a proanthocyandin- deplete extract (CGO 110) from plants of Family Euphorbaciae, specifically but not limited to the *Croton* species, such as *Croton lechleri*, also known as "Sangre de grado" (SdG) or "Dragon's Blood." This invention reduces the cytotoxicity of the parent ethnomedicine on normal cells, yet retains its ability to promote cancer cell death as well as its antidyspeptic, antiemetic, analgesic and antidiarrheal properties. By virtue of its reduced proanthocyandin content, this invention is amenable to topical applications, alone and in combination with other solvents, as its discoloring properties are reduced.

BACKGROUND OF THE INVENTION

Sangre de grado or Sangre de drago, also known as "Dragon's Blood," is a viscous latex sap derived from the bark of various *Croton* species (*C. dracanoides, C. erythrochilus, C. gossypifilius, C. lechleri, C. palanostigma, C. sakutaris*) indigenous to the South American rainforests. This latex has a deep red or burgundy color that is attributed to its substantial proanthocyandin content, estimated to being approximately 90% of the solid constituents of the sap. Ethnomedically, the latex is topically applied for the treatment of pain and itching associated with insect bites and stings, as well as plant reactions. It is applied to the gums of patients after tooth extractions, is utilized as a vaginal wash in the case of excessive bleeding and in the treatment of herpes where it is applied directly. It is also applied to open wounds as an anti-infective and as a cicratrizant to accelerate the healing process. This latter effect may result from its constitutive taspine and crolechleric acid. It is taken internally for a variety of distressing gastrointestinal symptoms, including the treatment of diarrhea, ulcers, vomiting and gut inflammation, as well as throat infections, tuberculosis and rheumatism. Oral intake is also associated with the ethnomedical application for cancer.

These traditional applications within South America cultures are less likely to be used in the Western world because of several constraints. Primarily, its intense color limits its ability to be used topically; in addition it discolors clothing in a similar manner as red wine, another proanthocyandin rich extract. A means of reducing the pranthocyandin content (and hence color) of the latex whilst retaining its useful biological properties would represent a significant improvement over the traditional botanical and allow for more widespread application.

The proanthocyandins have been implicated as the mediators of Sangre de grado's antidiarrheal properties through the prevention of cAMP mediated epithelial secretion. However, recent evidence suggests that Sangre de grado attenuates these epithelial secretory mechanisms by preventing the activation of sensory afferent nerves that promote diarrhea, local inflammation, edema, as well process signals to the brain for pain, nausea and itching. Capsaicin, the active component of chili peppers, stimulates these sensory afferent nerves and Sangre de grado has been shown to impair capsaicin-induced epithelial secretion of electrolytes.

OBJECTS AND SUMMARY OF THE INVENTION

The latex or sap derived from the bark of the *Croton* species of the South American rainforests is associated with various ethnomedical applications including the treatment of cancer, diarrhea, gastrointestinal distress, pain and itching. While effective for these indications the traditional

ethnomedicine has undesirable effects that limit its use. This invention teaches that the reduction or removal of the proanthocyandin content of the parent material can address these undesirable effects. In doing so, this extract retains its ability to inhibit emesis and activation of sensory afferent nerves. It furthermore promotes cancer cell death, unlike the parent material, at concentrations that fail to promote cell death in normal cells. Thus, this reduced cytotoxicity while retaining its traditional properties signifies an improvement over the parent botanical.

REDUCED PROANTHOCYANDIN CONTENT AND COLOR REACTIONS

As shown in Figure 1, the extraction process depletes the proanthocyandin content compared to the parent material and confirmed by a reduction in absorbency in the 390 to 430 nm range. This wavelength for detection is in the visible range, representing a significant reduction in color of this organic extract compared to the parent material. While the presence of the proanthocyandins provides a rich burgundy color to the ethnomedicine, it also results in the generation of an intense "chocolate" color when combined with various base vehicles, including *Aloe barbadensis* (aloe vera) gel – and can thus act to stain various materials. In contrast, the mixture of the organic extract (CGO 110) with a similar base vehicle significantly reduces this color reaction which can be readily quantified spectrophotometrically.

Sange de grado has potential benefits as a topical applicant for various inflamed itchy and irritated dermatological conditions. However, its inherent color due to a high proanthrocyandin content and thus the generation of an intense coloring when combined with base vehicles hinders its use for these applications. As the proanthrocyandin content and thus coloring are significantly reduced, alone or in combination with other topical cremes, gels or base vehicles, the invention, CGO 110, signifies a marked improvement in the natural product and its uses.

EFFECTS OF THE ORGANIC EXTRACT ON SENSORY AFFERENTS

The prototypical activator of sensory afferent nerves is capsaicin, the pungent chemical found in chili peppers. Activation of these nerves leads to a multitude of responses including vasodilation (mediated by the release of neurotransmitters from these activated nerves that cause blood vessels to relax), inflammatory cell recruitment, edema, and the sensations of pain and itching.

To address whether CGO 110 retains its ability to suppress this activation, it was tested for the ability to inhibit capsaicin-induced increases in gastric blood flow. The experiment involved the

topical application of capsaicin to the mucosal surface of the stomach in anesthetized rats and mucosal blood flow measured by a Laser Doppler Flow meter. As indicated in Figure 2, the marked increase in mucosal blood flow induced by 300μM capsaicin was prevented by either the parent material, SdG, or its organic extract, CGO 110 deplete of proanthrocyandins at doses of 2 and 0.2 mg/ml, respectively. Thus, the organic extract described in this invention retains the ability to effectively prevent the activation of sensory afferent nerves.

EFFECTS ON EMESIS

SdG has been used for the treatment of a variety of intestinal complications including diarrhea, ulcerations, cancer and emesis. Using a well-established ferret model of emesis, the organic extract CGO 110 was administered intraperitoneally (3mg/kg) to ferrets 15 minutes prior to the administration of morphine-6-glucuronide (M6G), a known agent used to promote both retching and vomiting, and the animals monitored for sixty minutes. In the control group, the subcutaneous injection of 0.05mg/kg M6G caused a significant number of vomiting and retching incidences while in those animals treated with CGO 110, the number of these episodes was virtually abolished. Given the utility of this model to predict treatments for nausea and vomiting, it is clear that this organic extraction procedure contains active components and is effective in the treatment of emesis.

CYTOTOXICITY: CANCER CELL SELECTIVITY

While Sangre de grado has traditional uses in the treatment of cancer, its utility is limited because it is equally toxic to both normal and cancerous cells. A process that could retain the ability of Sangre de grado to kill cancer cells but prevented these toxic effects on normal cells would represent a significant improvement over the traditional medicine and a benefit to the treatment of disease in both humans and animals.

To test the selective cytotoxic ability of CGO 110 *in vitro*, cancerous cells from the gastrointestinal tract (AGS: stomach) and both normal macrophages and normal intestinal epithelial cells (IEC-18) were utilized. Cancerous GI cells were chosen based on Sangre de grado's traditional application for gastrointestinal complications. Cell death was determined by the MTT assay [3-(4,5-dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide], which assesses cell number by virtue of its oxidative or respiratory activity and the generation of a dye detectable at a wavelength of 550 nm.

As shown in Figure 3, in normal cells, Sangre de grado caused significant cell death in both

macrophages and IEC-18 cells while the same concentrations of the organic extract CGO 110 did not. From this we can determine that the lipidic extract CGO 110 has improved safety over the parent botanical. Treatment of stomach cancer cells (AGS) with both CGO 110 and Sangre de grado caused cytotoxicity (cell death), and the lipidic extract, CGO 110, was more potent than the parent botanical [the "* " in Figure 3 denotes a significant difference between the Sangre de grado and organic extract CGO 110 formulations ($P<0.05$)]. Collectively, these results indicate that CGO 110 is selectively cytotoxic to cancerous cells compared to the parent botanical, thereby representing a marked improvement in safety.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

EXTRACTION PROCEDURE

This extraction technique concentrates the lipophilic components of the parent material whilst depleting it of hydrophilic proanthocyandins, and hence its intense burgundy color, making it more amenable to topical preparations. Furthermore, the product of this lipidic extraction, CGO 110, is selectively cytotoxic to cancerous cells, unlike the parent material, representing an improvement in safety. Examples of methods to accomplish the aforementioned composition are but not limited to the following:

EXAMPLE 1

Latex, or sap from *Croton* species is mixed with ethyl acetate in 1:1 proportion. Following agitation, the mixture is allowed to settle into its distinct phases and the organic phase (ethyl acetate, the top layer) is separated from the aqueous layer. It is common to find a gel-like substance appearing at the interface of the water and organic layers. This gel substance is of a dark brown and purple color and represents hydrophilic constituents trapped with water in the organic layer. This contaminant gel is removed by the addition of a drying agent (for example magnesium sulfate 0.5 – 5 g/L). This results in a precipitant which traps water and water-based colored chemical contaminants, which can be effectively removed by filtration through a Whatman #4 filter paper. The filtered organic layer clear of hydophilic contaminants is a rose color. The same steps of organic extraction, mixing with a drying agent and filtration is repeated up to three times to ensure complete extraction of the active constituents. Solutes contained within the organic solvent are concentrated by evaporation of the solvent by one of several procedures, such as vacuum drying, freeze drying or heating (up to 60 degrees C)..

EXAMPLE 2

The latex from the *Croton* species is dried to its residual solid matter by methods such as heating, air-drying, vacuum or freeze-drying. To this dark burgundy solid matter the organic solvent, ethyl acetate, is added. The mixture is agitated and the organic solvent is removed. This process is repeated up to three additional times to adequately extract all lipophilic materials. If any water bearing contaminants are present, the addition of drying agent followed by filtration as noted above, will remove these contaminants. Removing the ethyl acetate through various methods including heating, air-drying, vacuum or freeze-drying then isolates the solutes contained within this organic extract.

EXAMPLE 3

The procedure employed in Examples 1 or 2 is duplicated with the exception that the organic solvent is isopropanol or a chloroform/Methanol mixture as opposed to ethyl acetate.

While the invention has been described with reference to specific preferred embodiments, the invention is certainly not limited to those precise embodiments. Rather, many modifications and variations will become apparent to persons skilled in the art without departure from the scope and spirit of the invention, as defined in the appended claims.

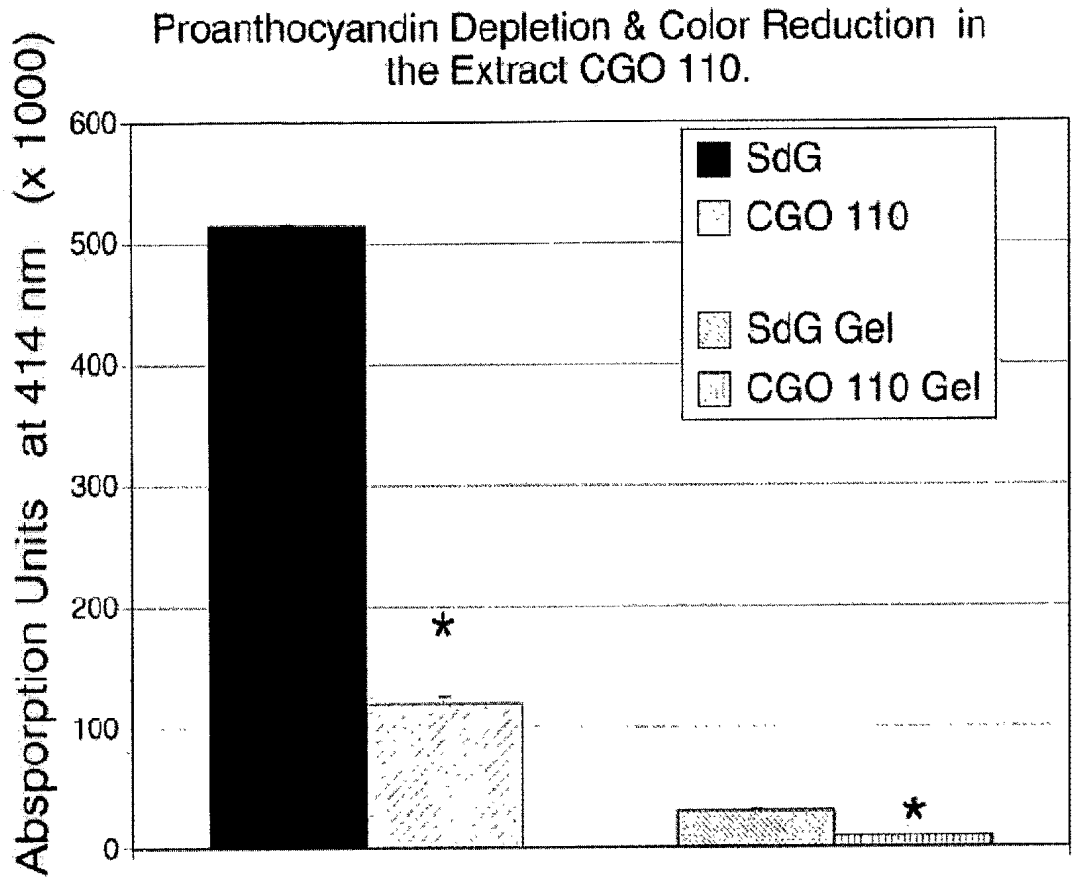

FIGURE 1: The extraction process significantly ("*") reduces the proanthocyandin content of the parent latex (SdG). When combined in a base vehicle, such as *Aloe barbadensis* shown here, the extract (CGO 110) produced a mixture absent of the intense color seen in similar preparations with the parent latex. This change, which is readily quantifiable by spectrophotometer, negates the discolorizing (i.e. staining) properties commonly associated with proanthocyandins and the parent latex and allows for practical dermatological preparations.

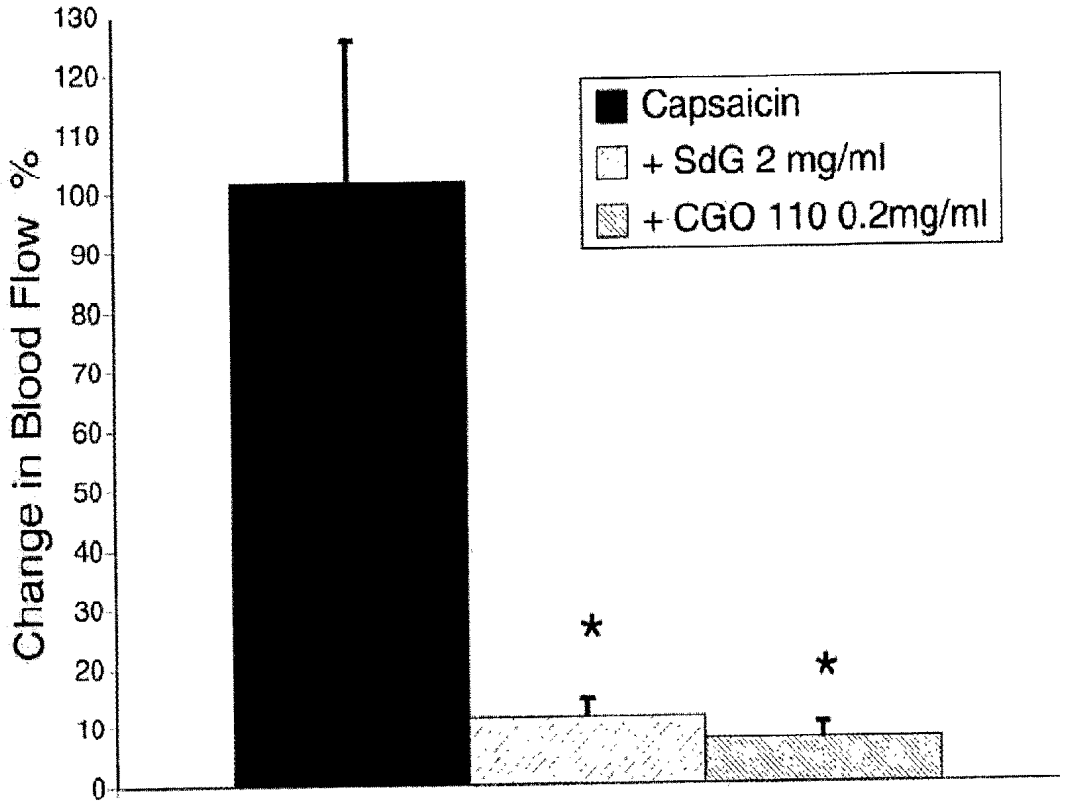

FIGURE 2: The prototypical activator of sensory afferent nerves, capsaicin, was topically applied to the mucosal surface of the stomach in anesthetized rats and mucosal blood flow measured by a Laser Doppler Flow meter. The marked increase in mucosal blood flow induced by 300μM capsaicin was prevented by either the parent material, SdG, or its organic extract, CGO 110 deplete of proanthrocyandins at doses of 2 and 0.2 mg/ml, respectively, indicating that the organic extract retains the ability to effectively prevent the activation of sensory afferent nerves.

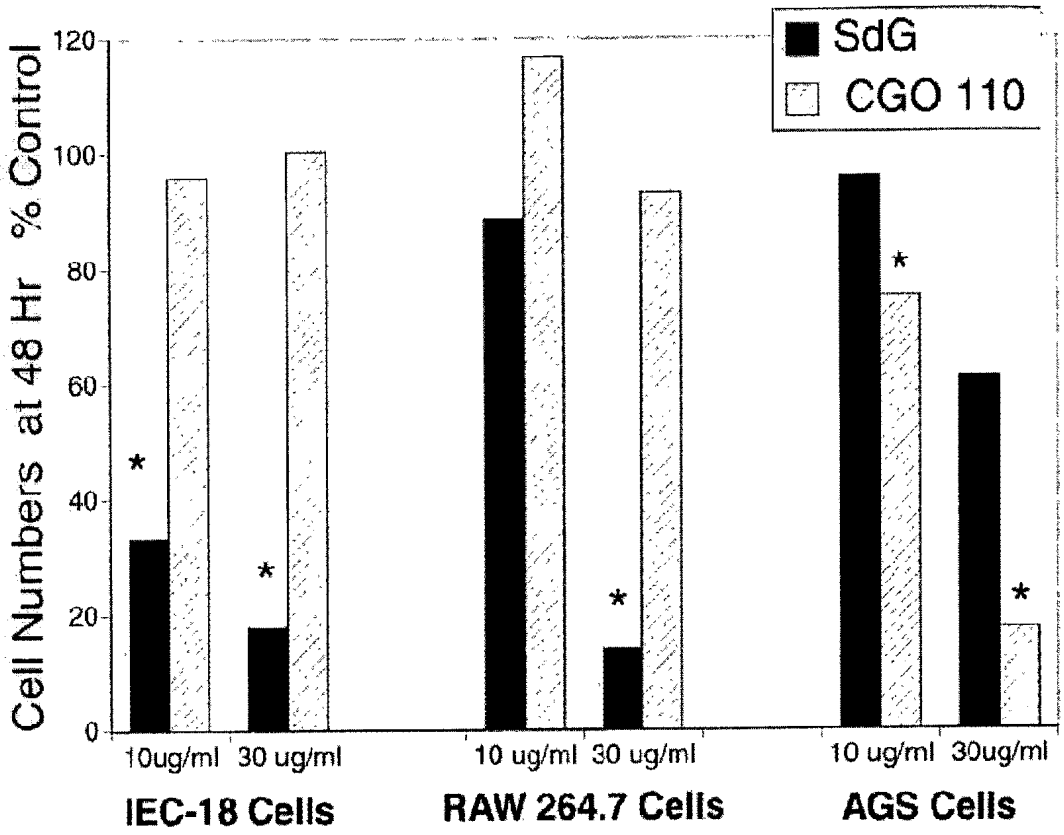

FIGURE 3: The selective cytotoxic ability of CGO 110 was tested *in vitro* in cancerous cells from the gastrointestinal tract (AGS: stomach) and also in both normal macrophages and normal intestinal epithelial cells (IEC-18). In normal cells, Sangre de grado caused significant cell death in both macrophages and IEC-18 cells while the same concentrations of the organic extract CGO 110 did not. In stomach cancer cells (AGS), both CGO 110 and Sangre de grado were cytotoxic and the extract was more potent than the parent botanical (the "* " in Figure 3 denotes a significant difference between the Sangre de grado and organic extract CGO 110 formulations ($P<0.05$). These results indicate that CGO 110 is selectively cytotoxic to cancerous cells compared to the parent botanical, and represents a marked improvement in safety.